Neonate with Annular Plaques of the Scalp

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Case Report

A two-month-old girl with no past medical history presented to the outpatient dermatology clinic with a rash on the scalp and forehead that had developed at two weeks of age and recently worsened. The patient's mother reported a normal spontaneous vaginal delivery without any complications, except for mild hyperbilirubinemia, which was subsequently treated with phototherapy. Upon discharge, the patient developed an asymptomatic rash beginning behind the left ear and progressed to involve most of the scalp and forehead. Readmission to the hospital led to a comprehensive workup for infectious causes, but no abnormalities were found. Consultation and a physical examination by the dermatology service revealed annular, erythematous plaques with central scale and crust on the forehead, scalp, and posterior neck (Figure 1). Some of the plaques appeared urticarial and targetoid with central duskiness and crusting (Figure 2). A review of systems was noncontributory. Laboratory assessments were sent and a skin biopsy for histological analysis was taken from the posterior left ear (Figures 3–5).

Diagnosis

Neonatal lupus erythematosus

Microscopic Findings and Clinical Course

The biopsy from the posterior left ear demonstrated an interstitial lymphoid and histiocytic dermatitis with interface change (Figures 3–5). Alcian blue stain revealed increased dermal mucin (Figure 6). Together, these histological features were suggestive of a collagen vascular disease. Laboratory evaluation revealed a positive anti-nuclear antibody (ANA) titer of 1:640 with both homogenous and nucleolar patterns as well as Sjögren's antibody positivity (anti-SSA/Ro, 5.50; anti-SSB/La, >8.00). Cardiac evaluation with electrocardiography (ECG) and echocardiogram (ECHO) revealed no abnormalities. The mother is currently being evaluated for the possibility of a systemic autoimmune disease.

Discussion

Neonatal lupus erythematosus (NLE) is a rare, benign, autoimmune disease caused by maternal autoantibodies that cross the placenta during pregnancy. First reported in 1928 in an infant born from a mother with Mikulicz's disease (a benign enlargement of the parotid gland often related to Sjögren's syndrome), NLE primarily manifests with cutaneous and cardiac findings.[1] This is in contrast to systemic lupus erythematosus (SLE), which presents with hepatobiliary, hematological, or neurological findings (Table 1). The presence of maternal autoantibodies, anti-SSA/Ro, anti-SSB/La, and/or U1-ribonucleoprotein (U1-RNP) is shown in NLE; anti-Ro antibodies are positive in 95 percent of cases.[2,3] Cutaneous manifestations are associated with maternal serum anti-SSB/La antibodies, with two-thirds of cases occurring at birth and the remainder of cases occurring in the first 2 to 5 months of life.[4] While not certain, NLE appears to occur in 1 in 20,000 live births, affecting all ethnicities, and is more common in female than male neonates (3:1).[5]

The typical clinical presentation of NLE consists of papulosquamous, annular, or elliptical plaques with central clearing on the face (in a periorbital distribution), scalp, trunk, and/or extremities. Similar to subacute cutaneous lupus erythematosus (SCLE), NLE lesions may appear as confluent or polycyclic, annular, scaly plaques, or as erythematous, infiltrated, urticarial plaques with central vesicles. These lesions often resemble nummular eczema, impetigo, or dermatophytosis.[6,7]

The clinical course of NLE is usually benign; skin lesions are nonscarring and typically disappear with the clearance of the maternal antibodies in six months. Only 10 to 25 percent of infants affected by NLE show residual skin anomalies, such as skin atrophy, telangiectasias, dyspigmentation, pitting, and/or atrophy. Sjögren's antibodies and ANAs increase photosensitivity due to activation of sequestered epidermal

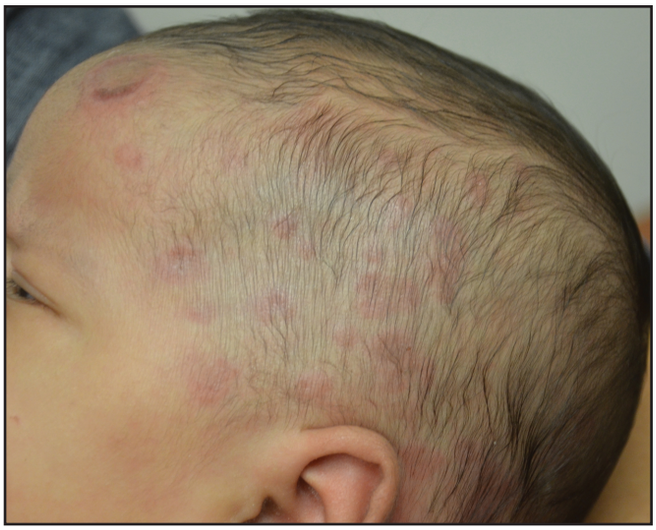

Figure 1. Annular and urticarial plaques on the scalp and forehead

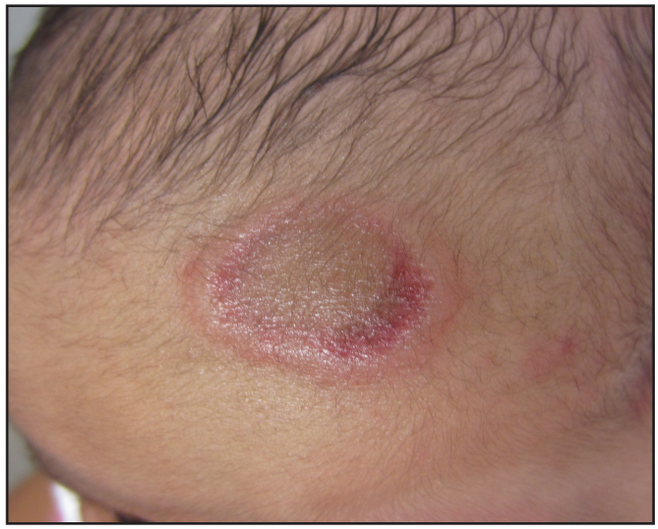

Figure 2. Annular plaque with central crusting on the forehead

antigens and cytokine release. As a result, exposure to ultraviolet (UV) light typically exacerbates NLE.[8–10]

While the skin manifestations are limited, the cardiac manifestations of NLE are potentially life threatening and can first be detected by fetal ultrasound at 20 to 24 weeks of gestation. There is an incidence of 15 to 30 percent of developing a cardiac anomaly due to NLE, which can range from varying degrees of heart block to cardiomyopathies. NLE accounts for 85 percent of all the cases of congenital complete heart block.[11]

The pathogenesis of heart block and cardiomyopathy is due to both the inflammation mediated by anti-SSA/Ro and SSB/La antibodies as well as direct endocardial and myocardial damage. Specifically, these antibodies cause progressive worsening fibrosis of the atrioventricular (AV) node, which is clinically detected as heart block.[12,13] The morbidity and mortality of congenital complete heart block is significant. Sixty-five percent of the surviving neonates require pacemakers with a mortality rate of 20 percent in the following three years of life.

The differential diagnosis is vast; however, photosensitivity and early age of onset can help distinguish NLE from other annular, urticarial, or papulosquamous disorders. The main feature that differentiates NLE from other photosensitive genodermatoses, in addition to a lack of other physical anomalies, is the presence of anti-SSA/Ro, anti-SSB/La, or anti-U1-RNP antibodies. Polycyclic skin lesions can be mistaken for urticaria, erythema marginatum, seborrheic dermatitis, psoriasis, atypical erythema multiforme, and mastocytosis. Urticaria is generally transient, slightly pruritic, and appears in differing locations; while seborrheic dermatitis is red, scaly, and crusty in fixed locations, such as the scalp, eyebrows, nasolabial folds, intertriginous areas, or chest. Intertriginous involvement helps differentiate NLE from Langerhans cell histiocytosis (LCH) and seborrheic dermatitis.

Additionally, mastocytosis is worsened by rubbing or scratching and may be accompanied by systemic symptoms. Isolated annular erythematous plaques should always raise suspicion of annular erythematous dermatoses, such as annulare centrifugum or erythema marginatum. Further, annular plaques with scale should be evaluated with a potassium hydroxide (KOH) preparation to rule out tinea infections. Family history, age of onset, a negative KOH test, and negative antibody detection may suggest a diagnosis of early psoriasis or atopic dermatitis. Erythema multiforme is often targetoid with violaceous centers that commonly presents on extensor surfaces and includes the palms and soles; although, atypical presentations are also common.[14]

The diagnosis of NLE is obtained by a combination of clinical suspicion, laboratory evaluation, and skin biopsy. Laboratory investigation includes a complete blood count (CBC), ANA, anti-double stranded deoxyribonucleic

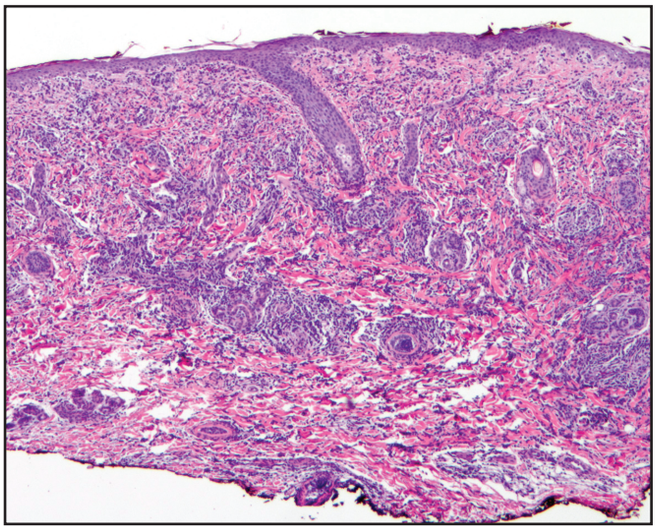

Figure 3. A superficial and deep perivascular, periadnexal, and interstitial lymphohistiocytic infiltrate is seen at low power (H&E x40)

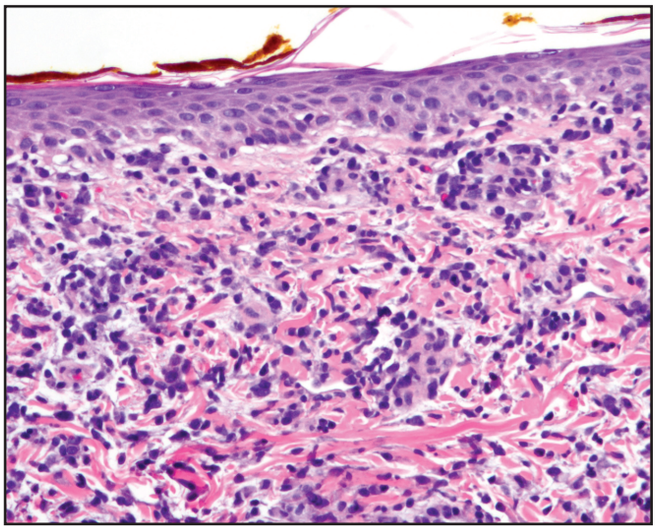

Figure 4. Interface changes at the dermal-epidermal junction (H&E x200)

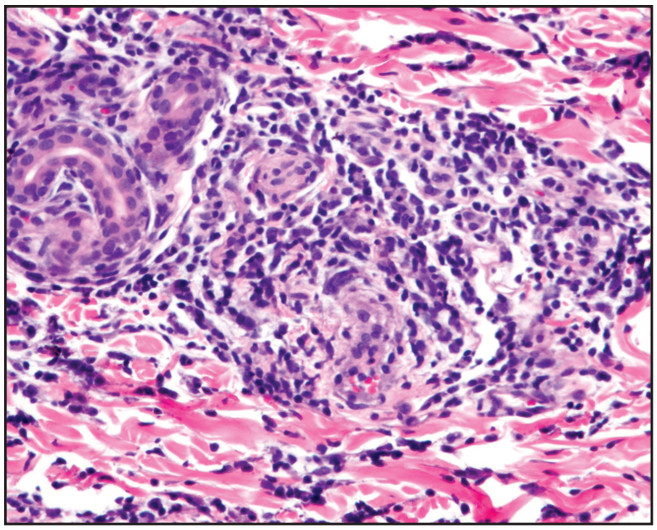

Figure 5. Lymphohistiocytic infiltrate concentrated around adnexa and glands (H&E x400)

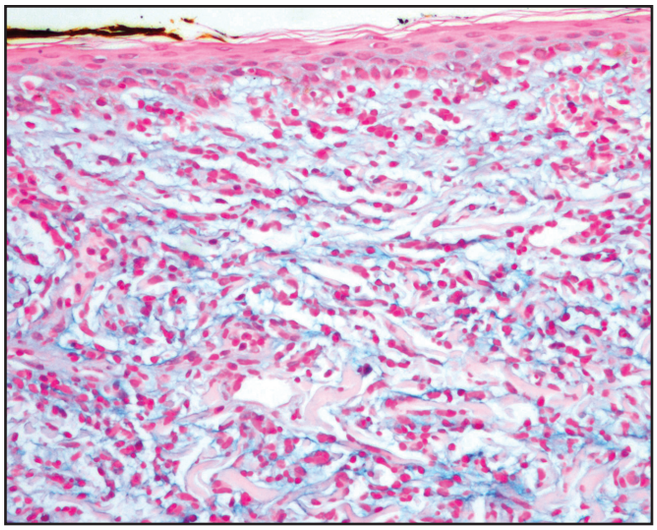

Figure 6. Alcian blue stain with increased dermal mucin (Alcian Blue x200)

acid (DNA), anti-Smith, anti-U1-RNP, anti-SSA/Ro, and anti-SSB/La antibodies. Reduced complement levels, specifically C2, C3, C4, and CH50, should also be obtained to confirm NLE. A complete metabolic panel (CMP) and urinalysis with microprotein analysis should be performed to search for end-organ dysfunction. Maternal evaluation should include similar testing, even if the patient is asymptomatic.

Histological analysis of cutaneous lesions should undergo both hematoxylin and eosin stain (H&E) and direct immunofluorescence (DIF). The typical histological findings of NLE are vacuolar degeneration in the basal cell layer of the epidermis and dermal mucin deposition. DIF demonstrates granular immunoglobulin G (IgG) and some IgM and C3 deposition at the dermal-epidermal junction.[15] The skin biopsy of the patient described in this

TABLE 1. Differences between neonatal and systemic lupus erythematosus[6,14,19]

	NEONATAL LUPUS ERYTHEMATOSUS	SYSTEMIC LUPUS ERYTHEMATOSUS
Etiology	Multifactorial; autoantibody production, genetic susceptibility, environmental stimuli, and medications	Systemic lupus erythematosus
Onset	At birth or by 2 to 5 months of life	Peaks after puberty to adulthood
Course	Typically resolves spontaneously by six months	Chronic, relapsing, remitting course
Antibodies	Maternal autoantibodies of anti-SSA/Ro and anti-SSB/La	ANA, dsDNA, Sm, antiphospholipid
Prevalence	Rare; 1 in 20,000; both cutaneous and cardiac findings more common in females; no racial predilection	5 per 100,000; more common in African American females
Clinical features	Mostly cutaneous, cardiac, hepatic, hematological findings	Multisystem disease; symptoms will reflect the system affected
Cutaneous findings	Annular erythematous, polycystic plaques with fine scale on neck, scalp, face, periorbitally; may resemble SCLE	Discoid and malar lesions; plaques with follicular plugging, hyperkeratosis, dyspigmentation, scarring, and/or erythematous patches; more common in sun-exposed areas
Cardiac findings	Heart block (incomplete or complete)	Pericarditis, myocarditis, and pulmonary hypertension
Prognosis	Benign, resolves spontaneously; increased risk of developing life-long cardiac disease	Incurable, but treatable; varies from benign disease to rapidly progressive and fatal
Prophylaxis	Topical and/or oral corticosteroids, antimalarials, sunprotection; intravenous immunoglobulin for mothers to reduce risk in subsequent births	Topical and/or oral corticosteroids, antimalarials, oral retinoids, systemic immunosuppressants; sun protection is essential

case demonstrated a perivascular and interstitial lymphohistiocytic infiltrate with interface change and increased dermal mucin; the histopathology of which more closely resembles that of SCLE.[16]

Treatment of NLE is supportive and includes the involvement of multiple specialties. Most times, skin findings resolve in 2 to 6 months after birth as the infant clears the maternal antibodies. If symptomatic, lesions can be treated with topical corticosteroids and antipruritic creams. Should symptoms continue to persist, antimalarial medications can be added to the treatment regimen. Systemic immunosuppressives and/or corticosteroids are typically avoided unless there is hepatic, renal, or hematological disease.[15] Sun protection is essential with broad-spectrum coverage, as the skin becomes particularly photosensitive. Maternal monitoring is crucial because there is a 25-percent risk of fetal development of NLE in

subsequent pregnancies.[17,18] Interestingly, mothers treated with oral corticosteroids and hydroxychloroquine have shown reduced rates of fetal heart block.[19] Thus, rheumatological evaluation, monitoring, and treatment should be obtained in a mother who gave birth to an infant with NLE. Because cardiac manifestations can occur later in the infant's life, proper cardiac follow-up is also critical.

Conclusion

In order to avoid potential complications of NLE, a multidisciplinary team of providers for the mother and child is encouraged. NLE is confirmed primarily by histological analysis and specific antibody positivity. Although skin, hematological, and hepatic manifestations often resolve spontaneously in the first six months of life, the risk of heart block continues and is the most significant risk of mortality. Pregnant antibody-positive mothers should be monitored throughout pregnancy and counseled regarding subsequent pregnancies and the risk of passing autoimmune disease. Patients affected should have regular follow-up visits until adolescence, even if skin lesions resolve spontaneously in the first year or if there is no evidence of cardiovascular disease. Although rare, a diagnosis of NLE by a dermatologist or pediatrician can impact the future life-long care of both the mother and child affected. NLE should be considered in the differential diagnosis of a persistent, annular rash in a newborn or neonate.

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